Atrial Fibrillation: An Underestimated Cause of Ischemic Monocular Visual Loss?

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Introduction: Atrial fibrillation (AF) is a major cause of ischemic stroke and Transient Ischemic Attack (TIA) and investigation for paroxysmal AF is recommended following an embolic brain event. In contrast, retinal ischemic monocular blindness is traditionally considered most linked to carotid artery disease (CAS) and investigating for AF is less vigilant. We aimed to determine the prevalence of AF in patients with ischemic monocular blindness. *Methods:* Consecutive records of all patients presenting to a daily TIA clinic with transient or permanent ischemic monocular blindness were reviewed, January 2014-October 2016. *Results:* Of 400 patients, 224 (56.0%) were male, mean age 64.5 years (SD 15.1). A total of 263 (66%) presented with transient and 137 (34%) with permanent ischemic monocular blindness. ECG was performed in 364 patients (91%) but only 211 (52%) had further cardiac monitoring. The vast majority (97.3%) had carotid imaging. Thirty-six patients (9%) were found to have AF while 53 (14%) had ipsilateral CAS. Median ABCD2 score was 1 in AF and non-AF groups. Only 55% of known AF patients were anticoagulated at presentation, despite all having CHADVASC2 score greater than or equal to 1. Patients with AF had more hypertension ($P = .004$), previous TIA ($P = .002$), previous stroke ($P = .044$) and ischemic heart disease ($P = .022$) with no difference in age ($P = .791$), diabetes ($P = .563$), smoking ($P = .460$) nor hypercholesterolaemia ($P = .083$). *Conclusions:* A total of 9% of patients with ischemic monocular blindness had AF. This is an underestimate, as only 53% of patients had prolonged cardiac monitoring. Known AF was suboptimally managed with only 55% receiving anticoagulation despite being eligible.

Key Words: Ischemic monocular visual loss—atrial fibrillation—transient ischemic attack—retinal artery occlusion

Introduction

Acute retinal ischemia, due to transient or permanent occlusion of the central or branch retinal artery is a major cause of monocular visual loss and a significant presentation of cerebrovascular disease.[1] Causes of ischemic retinal monocular visual loss are similar to those of ischemic stroke which can be classified according to the TOAST system, as large-artery atherosclerosis, cardioembolism, small-vessel occlusion, stroke of other determined etiology, and stroke of undetermined aetiology.[2]

Atrial fibrillation (AF) is a recognized cause of cardioembolism associated with a 5-fold increase in the risk of stroke.[3] Prolonged cardiac monitoring rather than simple ECG is usually required to detect paroxysmal AF;[4] this has led to the incorporation of prolonged rhythm monitoring amongst necessary investigations in patients with acute stroke in European and American guidelines. However, patients with ischemic monocular visual loss, which is traditionally considered to be secondary to carotid artery disease rather than cardioembolism, are often less vigorously investigated for AF.

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We aim to determine vascular risk factors and the prevalence of AF as the cause of ischemic monocular visual loss.

Methods

Patient Selection

We retrospectively reviewed the records of all consecutive patients seen in the hyperacute, daily TIA clinic and hyperacute stroke unit at University College London Hospital between January 2014 and October 2016. All patients with ischemic monocular visual loss secondary to retinal ischemia were included. Patients with a diagnosis of ischemic optic neuropathy or giant cell arteritis were excluded. Our referral pathway was via Moorfields Eye Hospital, London, where patients received a comprehensive ophthalmological assessment; ocular causes of visual loss were excluded prior to referral to our clinic.

Transient ischemic visual loss (TVL) was defined as monocular visual loss of part or whole of the patient's visual field, lasting less than 24 hours. Permanent ischemic visual loss (PVL) was defined as monocular visual loss, due to central or branch retinal artery obstruction, lasting more than 24 hours. The TOAST causative classification for stroke was used to clarify clinical subtypes.[5]

Assessment of Vascular Risk Factors and Recurrent Events

Included patients' records were reviewed for the presence of vascular risk factors including diabetes, hypertension, previous ischemic stroke or transient ischemic attack (TIA), previous TVL or PVL, previous myocardial infarction (MI), hypercholesterolaemia, AF, and current or past smoking.

Repeat hospital attendances with recurrent cerebrovascular events until October 2016 were recorded. Recurrent events were defined as TIA, ischemic stroke, TVL, PVL, and MI, occurring within 90 days from initial presentation. We reported on recurrence rate within 90 days, to ensure that data on recurrences were available for all patients included in our cohort. To capture the true recurrence rate and avoid underestimates, we included recurrent events that occurred prior to the review of patients in our clinic.

Following clinic review, all included patients received antiplatelet and statin treatment. Only imaging, echocardiogram and cardiac monitoring data where reports were available at the time of the study were included in the analysis. Symptomatic carotid artery disease (CAS) was defined as presence of stenosis of the ipsilateral to the symptoms carotid artery of equal to, or more than, 50%, the limit for consideration of carotid endarterectomy.

Statistical Analysis

Statistical analysis was performed using R.3.2.2 for Windows (R Foundation for Statistical Computing). Patients with missing data were excluded from relevant analyses. Pearson's uncorrected chi-square test and Fisher's exact test were used depending on sample size. Statistical significance was defined as $P < .05$.

Results

Four-hundred patients with ischemic monocular visual loss were included, mean age was 64.5 years (SD = 15.1, range 18-94) and 224 (56%) were male. Presentations with TVL were more common (263 patients, 66%). Average blood pressure was 140/77 mmHg. ABCD2 score at presentation was available, or possible to calculate from the records, in 297 patient and median score was 2 (range 1-6). Premorbid vascular risk factors were recorded: HTN 51%, hypercholesterolaemia 35%, diabetes 15%, ischemic ocular events 12%, ischemic heart disease 10%, TIA 6%, stroke 5%, and smokers 12%. Patients presenting with PVL had increased prevalence of diabetes (21% versus 11%, $P < .001$), HTN (64% versus 45%, $P = .008$) and ischemic heart disease (16% versus 7%, $P = .005$). Demographics are presented in Table 1.

Twenty-nine patients had known AF (8%); this did not differ between patients with PVL and TVL. All patients with known AF had a CHADVASC2 score of 1 or more. Only 16 (55%) of these patients were anticoagulated at

Table 1. *Baseline characteristics*

	n (%)
Age (average) years	64.5
Male	224 (56.0)
Blood pressure on arrival (mean)	
Systolic	140 (92-208)
Diastolic	77 (42-124)
ABCD2 (median)*	2 (1-6)
n = 297	
Diabetes mellitus	58 (14.5)
Hypertension	205 (51.3)
Previous stroke	21 (5.3)
Previous MI	40 (10.0)
Previous TIA	25 (6.3)
	47 (11.9)
Previous ocular events	47 (11.8)
Hypercholesterolaemia	141 (35.3)
Previous AF	29 (7.3)
Smoking (ex and current)	138 (34.5)
Current smoking	49 (12.3)
Cause of Ischemic visual loss	
Large artery atherosclesoris	121 (30.3)
Cardioembolic	51 (12.8)
Small artery occlusion	24 (6)
Other	2 (.5)
Indeterminate	187 (46.8)

AF, atrial fibrillation; MI, myocardial infarction, TIA, transient ischemic attach.

*Unable to calculate for 103 patients (25.8%) due to 1 or more item missing.

presentation and 7 (24.1%) were on antiplatelet treatment. Six (21%) were not on any treatment.

In total, 339 (85%) had brain imaging. The vast majority, 389 (97%) had imaging of the carotid arteries, either a CT angiogram (55%) or carotid doppler (57%). An ECG was performed on 364 (91%), however only 237 (59%) were referred for prolonged cardiac monitoring to assess for AF. Results were available at the time of the study for 161 (40%). Echocardiogram was performed in 228 (57.0%) and results were available at the time of the study for 155 patients (39%).

Fifty-three (14% of those scanned) had symptomatic CAS; patients presenting with PVL had higher prevalence of symptomatic CAS (20% versus 11%, $P = .015$). Thirty-six had AF. In 7 patients this was a new diagnosis; all new cases were identified after prolonged cardiac monitoring (at least 24 hour recording); 4% of patients who had prolonged cardiac monitoring had AF. The investigations for CAS and AF are presented in Table 2.

Patients with AF were more likely to have coexisting HTN ($P = .004$), previous TIA ($P = .002$), previous stroke ($P = .046$), and previous MI ($P = .022$). Although there was no difference in the prevalence of symptomatic CAS in patients with AF, patients with AF were more likely to have contralateral CAS greater than or equal to 50% ($P = .044$).

The cause of stroke was attributed in large artery atherosclerosis in 121 patients (30%), cardioembolic in 51 (13%), small artery occlusion 24 (6%) and other 2 (0.5%), while in 197 patients (49%), it was indeterminate; the high proportion of indeterminate cause could be due to carotid imaging and cardiac monitoring results not being available at the time of the study.

Ninety-day recurrence of stroke/TIA/ocular ischemia was 10.5% (42 events). This was higher in AF patients (19.4%, mean 12.3 days, median 7) and comparable to patients with CAS (18.9%). Patients with AF were more likely to represent with stroke (hazard ratio = 5.74, 95% confidence interval = [0.54, 61.6], $P = .652$). The differences in risk factors and recurrence in patients with and without AF are seen in Table 3.

Discussion

Traditionally, ischemic retinal monocular visual loss is thought to be caused by ipsilateral CAS rather than AF and cardioembolism, contrary to cerebral ischaemia.[6]

However, rates of AF and CAS were comparable in our cohort. Almost 1 in 10 patients presenting with monocular ischemic visual loss had AF, higher than the expected prevalence[7]; this is likely an underestimate due to poor rates of prolonged cardiac monitoring with only 55% referred. Other recent studies of retinal ischemia reported variable AF prevalence from 4% to 16%.[6,8,9] The variability in reported AF might stem from different methods of recording and lack of prolonged monitoring. In our cohort, all new AF diagnoses were made on prolonged monitoring and missed on single 12-lead ECG; this is in keeping with a recent study by Callizo et al, showing significant increase in AF detection with each day of cardiac monitoring.[9]

It is well established that nonvalvular AF is an independent predictor of stroke[3] making its timely recognition and treatment an imperative part of secondary prevention, a fact reflected in recent guidelines. In our cohort, patients with AF were also more likely to have HTN, previous IHD and asymptomatic CAS, thus further increasing their cerebrovascular risk. Despite this, only 55% of patients with known AF were receiving anticoagulation.

Although not reaching statistical significance, patients with AF had a higher 90-day recurrence rate, with total recurrence rate of 11%, higher than previously reported in monocular ischemic visual loss.[10,11] Given that early investigation for vascular risk factors and treatment after TIA significantly reduces the risk of early recurrent stroke,[14] presentation with monocular ischemic visual loss represents an important opportunity for secondary prevention, particularly regarding AF. We propose that prolonged cardiac monitoring should be incorporated in the diagnostic work-up of all patients presenting with ischemic monocular visual loss, similarly to other TIA or stroke, given the vital importance of early identification and treatment of AF to secondary stroke prevention.

Our study included a large number of patients from a single center over 2 years, all similarly managed. In contrast, most published cohorts of monocular ischemic visual loss so far included smaller numbers, or recruited for longer period of time, resulting to heterogeneity of investigations and management.[8,10-13]

There are several limitations. First, this was a retrospective review which limits the available recorded information; similarly, recurrent events may have been underestimated due to nonrecording of out-of-area

Table 2. *Investigations performed to investigate possible embolic source*

Carotid artery disease (CAS) n (%)		Atrial fibrillation (AF) n (%)	
Any modality	389 (97.3%)	Any modality	392 (98%)
Doppler	226 (56.5%)	ECG	364 (91%)
CT angiogram	218 (54.5%)	Prolonged monitoring	161 (40.3%)
Patients with symptomatic CAS	53 (13.6%)	Patients with AF	36 (9.2%)

Table 3. *Risk factors and recurrence in patients with and without AF*

	Patients with AF n(%) n = 36	Total n(%) n = 400	*P* value
Demographics			
Age (average) years	75	64.5	.791
Male	22 (61.1)	224 (56.0)	.648
ABCD2 (median)	1	2	.285
Presentation with BCRAO	12 (33.3)	137 (34.3)	1
Risk factors			
Diabetes	7 (19.4)	58 (14.5)	.563
Hypertension	27 (75.0)	205 (51.3)	**.004**
Previous stroke	5 (13.9)	21 (5.3)	**.046**
Previous MI	8 (22.2)	40 (10.0)	**.022**
Previous TIA	7 (19.4)	25 (6.3)	**.002**
		47 (11.9)	
Previous ocular events	3 (8.3)	47 (11.8)	.660
Hypercholesterolaemia	18 (50)	141 (35.3)	.083
Current smoking	5 (13.9)	49 (12.3)	1
Carotid artery disease			
Symptomatic >=50%	5 (13.9)	53 (13.3)	1
Asymptomatic (contralateral) >=50%	5 (13.9)	21 (5.3)	**.044**
Previous history of AF		**29**	
On anticoagulation*		16	
On antiplatelets*		7	
No treatment*		6	
Recurrent events			
Total 90-day recurrences	7 (19.4)	41 (10.3)	.103
Stroke	2 (5.6)	5 (1.3)	.652
BRCAO	1 (2.8)	4 (1.0)	.817

AF, atrial fibrillation; BCRAO, branch/central retinal artery occlusion, CAS, carotid artery stenosis of the symptomatic side more than 50%, MI, myocardial infarction, TIA, transient ischemic attach.

*All patients had CHADVASC2 greater than or equal to 1.

events. Second, unlike immediate vascular imaging there were delays (time-to-holter and time-to-report) to cardiac monitoring. It would be useful to study AF rates with newer, timelier "patch" monitoring, a transdermal, noninvasive method of ECG recording. Thirdly, the utility of transthoracic or advanced echocardiography in our cohort is unclear, as only a proportion of patients in our cohort had an echocardiogram.

A prospective follow-up of patients presenting with monocular ischemic visual loss with both prolonged cardiac monitoring and transthoracic echocardiogram data, will help clarify the prevalence of AF, true recurrence rates as well as identify which risk factors affect recurrence in this population.

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